

CLAIMS

1. A retroviral vector production system for producing lentivirus-
5 based, replication defective vector particles for gene therapy, said vector
particles capable of infecting and transducing non-dividing mammalian target
cells, which system comprises a set of nucleic acid sequences encoding the
components of the vector, wherein one or more functional genes chosen
from the HIV-1 auxiliary genes *vpr*, *vif*, *tat* and *nef* or from the analogous
10 auxiliary genes of other lentiviruses, which auxiliary genes are normally
present in the lentivirus on which the vector particles are based, is or are
absent from the system.
2. The retroviral vector production system according to claim 1 for
producing HIV-1-based vector particles, wherein the functional auxiliary gene
15 *vpu* is also absent, with the proviso that when functional *vpu* and *vpr* genes
are both absent, so also is one or more of the auxiliary genes chosen from
vif, *tat* and *nef*.
3. The retroviral vector production system according to claim 1 or
claim 2, wherein functional *vpr* and *tat* genes or analogous genes normally
20 present in the lentivirus on which the vector particles are based are both
absent from the system.
4. The retroviral vector production system according to any one
of claims 1 to 3 for producing HIV-based vector particles, wherein three or
four or all five of the functional auxiliary genes *vpr*, *vif*, *tat*, *nef* and *vpu* are
25 absent from the system.
5. The retroviral vector production system according to any one
of claims 1 to 4, wherein a nucleic acid sequence encoding the RNA
genome of the vector comprises one or more therapeutically active genes.

- 20 -

6. The retroviral vector production system according to any one of claims 1 to 5, wherein the set of nucleic acid sequences encoding the components of the vector includes three DNA constructs which encode the RNA genome of the vector, *gag* and *pol* proteins, and *env* protein or a substitute therefor, respectively.

7. The retroviral vector production system according to any one of claims 1 to 6, wherein a nucleic acid sequence encoding the RNA genome of the vector comprises *rev* and RRE sequences or functional equivalents thereof, to enable export of transcripts of the genome from nucleus to cytoplasm.

8. The retroviral vector production system according to any one of claims 1 to 7, in a host cell.

9. The retroviral vector production system according to any one of claims 1 to 8, wherein all of the functional auxiliary genes normally present in the lentiviruses on which the vector particles are based are absent from the system, other than *rev* which is optionally present.

10. A DNA construct for use in the system according to claim 9, said DNA construct encoding a packagable RNA vector genome and operably linked to a promoter.

11. A DNA construct as claimed in claim 10, wherein the promoter is a non-retroviral, high efficiency promoter.

12. A set of DNA constructs for use in the system according to claim 9, comprising the DNA construct according to claim 10 or claim 11, and a DNA construct encoding *gag* and *pol* proteins.

13. A set of DNA constructs as claimed in claim 12, further comprising a DNA construct encoding *env* protein or a substitute therefor.

14. DNA constructs for use in the system according to claim 9, comprising the DNA constructs according to any one of claims 10 to 14, in one or more expression vectors.

- 21 -

15. A retroviral vector particle produced by the system according to any one of claims 1 to 9.
16. The use of a retroviral vector particle according to claim 15, for gene therapy for infection and transduction of a target cell.
- 5 17. The use of a retroviral vector particle according to claim 15, in the preparation of a medicament for use in gene therapy.
18. A method for performing gene therapy on a target cell, which method comprises infecting and transducing the target cell with a retroviral vector according to claim 15.
- 10 19. Target cells resulting from the use or method according to any one of claims 16 to 18.